DETAILED ACTION

Status of the Claims

1. Claims 4-12 are pending.

Response to Arguments

2. Applicant's response of 8/21/08 to the Non-Final rejection mailed out on 5/2/08 is acknowledged herewith.

a. In view of applicants cancellation of claims 1-3 the 112-2 paragraph rejection of claims 1-3 and the 35 USC 101 rejection of claims 1-3 is herein withdrawn. Newly added claims 4-12 are examined on their merits and the following FINAL rejection is made.

Drawings

3. Acknowledgement and acceptance are made of the 12 sheets of drawings filed on 05/04/2005. This has been reflected in PTO-326 accompanying this action.

Priority

4. Applicant's claim for the benefit of a prior-filed international application PCT/IT03/00626 (filed on 10/14/2003) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The effective filing date of the instant application is 10/14/2003.

5. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Italy on 11/06/2002. It is noted, however, that applicant has not filed a certified copy of

the IT RM2002A000562 application as required by 35 U.S.C. 119(b). Submission of a certified copy will be necessary to overcome an art rejection based on references published between 11/06/2002 and the effective filing date.

Information Disclosure Statement

6. Acknowledgement is made of receipt of International Applications WO 99/56737, WO 01/12228, and WO 01/08671.

Claim Rejections - 35 USC § 112 (1st paragraph)

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 10-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

9. *In re Wands*, 858 F.2d at 736-40, 8 USPQ2d at 1403-07, set forth eight factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (MPEP § 2164.01(a)) The relevant Wands factors are addressed below:

a. *The breadth of the claim*: Claims 10-12 are drawn to a method of preventing an influenza infection in a subject comprising the administration of a virus-inhibiting amount of resveratrol. Claims 11 and 12 limit the subject to be treated to a human (Claim 11) or a veterinary animal (Claim 12).

"Prevent" and "prevention" are potent terms implying that the method of prevention will necessarily prevent the influenza virus from infecting any cell in a subject at any point following administration of resveratrol. Accordingly, if even one cell becomes infected with influenza, the method is no longer considered a prevention method;

b. *Nature of the invention*: The nature of the invention is a method of treating a subject that is infected with the influenza virus comprising administration of resveratrol. The treatment results in the inhibition of influenza viral replication;

c. *The state of the prior art*: Resveratrol has been known to reduce HIV replication (Redfield, et al., US Patent No. 6,479,466, 2002, Figs 1 and 2). Examiner found no examples of resveratrol being an effective preventative measure of viral replication in general, or influenza replication in particular;

d. *Amount of direction provided by the inventor*: Applicant discloses that resveratrol exerts its anti-replication mechanism through inhibition of PKC;

e. *Existence of working examples*: Figure 1B discloses that resveratrol does not prevent influenza infection in MDCK cells, *in vitro*; and,

f. *Quantity or experimentation needed to make or use the invention based on the content of the disclosure*: Preventing an influenza infection requires that not one virus

infects any cell. Applicant has provided data indicating that treating cells that have been infected with influenza can inhibit further infection (Fig 1A). However, applicant has also demonstrated that pre-treating MDCK cells with resveratrol does not prevent the infection of cells with influenza. The prior art does not make up for the deficiencies. The combination of the instant specification and the prior art would not allow one of ordinary skill in the art to use resveratrol as a method to prevent influenza infection. Therefore, undue and unpredictable experimentation would be required to use the invention commensurate with the scope of the rejected claims.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heredia, et al. (Journal of Acquired Immune Deficiency Syndromes, 2000) in view of Kurokawa, et al (Journal of General Virology, 1990, and Pätzold, et al. (Antiviral Research, 1993).

13. Claims 4 and 7 are drawn to a method of inhibiting influenza virus replication (Claim 4) or treating an influenza infection (Claim 7) comprising administration of resveratrol. Claims 5 and 8 limit the subject to a human and the influenza virus to human influenza virus. Claims 6 and 9 limit the subject to a veterinary animal and the influenza virus to a veterinary virus infection.

14. Heredia, et al., teach that resveratrol can inhibit HIV-1 replication, *ex vivo* (Figures 1A and B, leftmost data points on each graph). Heredia, et al., also teach that resveratrol is "a widely used natural product," indicating that it is already safely used, *in vivo*, and is a known protein kinase C inhibitor (pg 247, col 1, final paragraph).

15. Heredia, et al., do not teach that resveratrol can inhibit influenza virus replication, or as a treatment for influenza virus infections, nor the role of PKC in HIV replication.

16. Pätzold, et al., teach that protein kinase C prevents replication of U1 cells latently infected with HIV (abstract).

17. Kurokawa, et al., teaches that the protein kinase C inhibitor H7 inhibits the replication of influenza (abstract).

18. Since both HIV and influenza are RNA viruses, one of ordinary skill in the art would reasonably expect that a molecule that inhibits HIV replication would also inhibit influenza replication. Moreover, the art teaches that both HIV and influenza require protein kinase C for replication, and one of ordinary skill in the art would reasonably expect that if inhibiting protein

kinase C inhibits replication of HIV, it would also inhibit influenza replication. Resveratrol is well known, and is currently been shown to effectively treat atherosclerosis and inflammation (Heredia, et al., abstract). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer a composition comprising resveratrol to inhibit influenza virus replication in a subject or treat an influenza infection in a subject.

Conclusion

19. No claims are allowed.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

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